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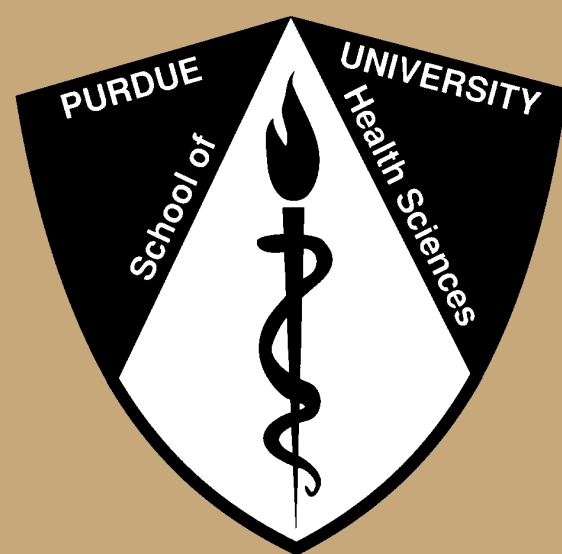


# Developing Drug Therapies for Cognitive Damage in Mice Following Brain Radiation



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## Introduction

Radiation is commonly used as an effective form of therapy when treating brain tumors. Like other therapies, radiation comes with risks of potential side effects. Pediatric brain cancer patients who survive are at a high risk for radiation-induced cognitive impairment in healthy tissue surrounding the tumor due to white matter changes in the brain. Unfortunately, about half of 6 month radiotherapy survivors develop significant changes in white matter, potentially leading to significant cognitive changes and impairment. To further investigate these effects, a mouse model of radiation injury was developed to investigate if mice that received brain radiation develop the same cognitive and behavioral changes as seen in human patients.

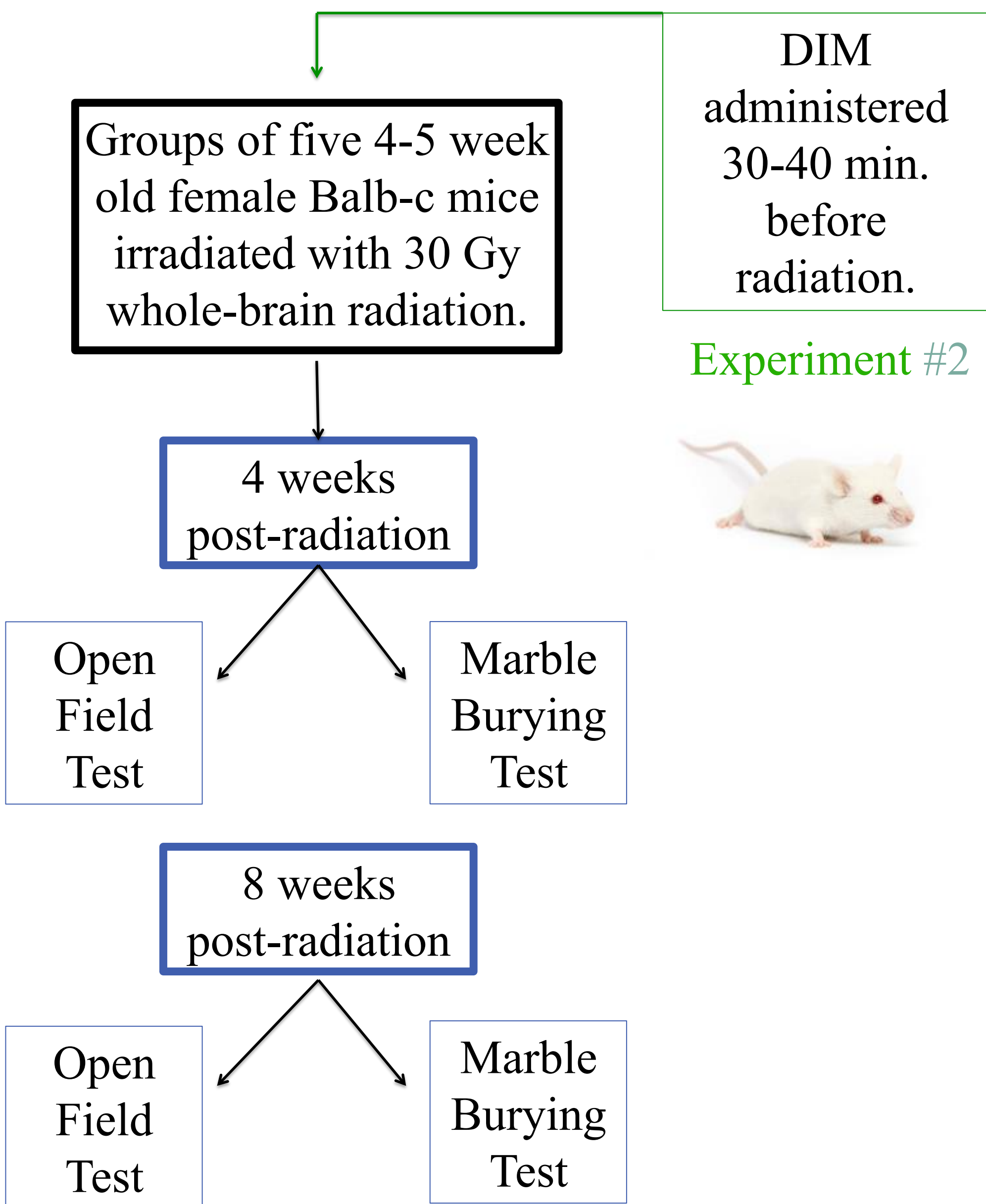
In previous experiments, pathology and behavioral tests proved that radiation injury can be modeled in mice to show significant impairments, and these deficits became more pronounced over time. **The purpose of this experiment was to investigate whether drug therapies, like Donepezil and 3,3-Diindolylmethane, (DIM), can be used in mice to reverse or protect from the cognitive damage that results from brain radiation.** Donepezil is a cognition-enhancing drug used to treat Alzheimer's patients and hypothesized to treat and reverse the effects of radiation injury. DIM is a chemical naturally formed in the body by breaking down cruciferous vegetables and thought to possibly protect from cancer. It is hypothesized to act as a radioprotectant.

## Methods

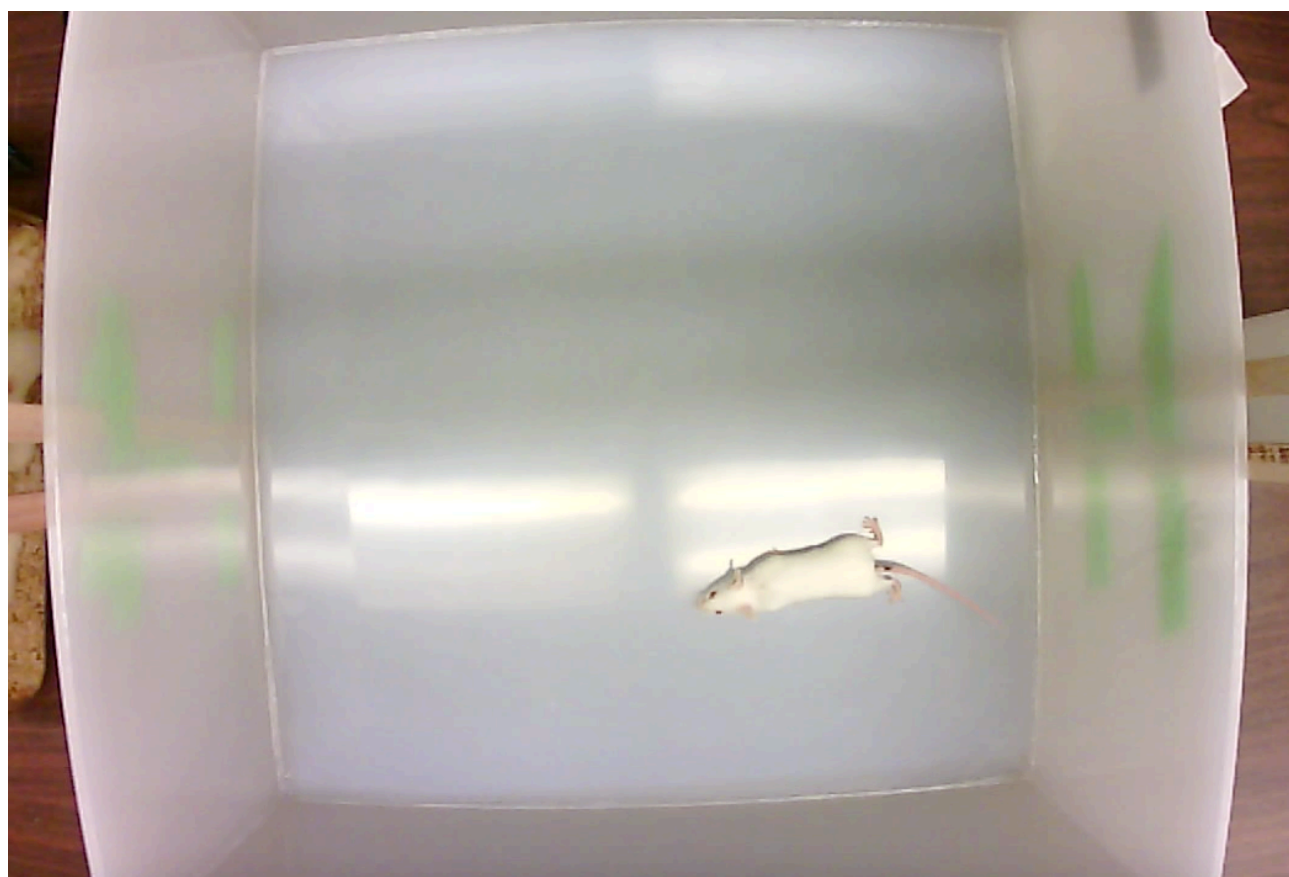


### Experiment #1

Donepezil administered 5x a week.



### Open Field Test



Normal mouse behavior:  
Spends even amount of time on center and outside of field over 20 min.

### Marble Burying Test

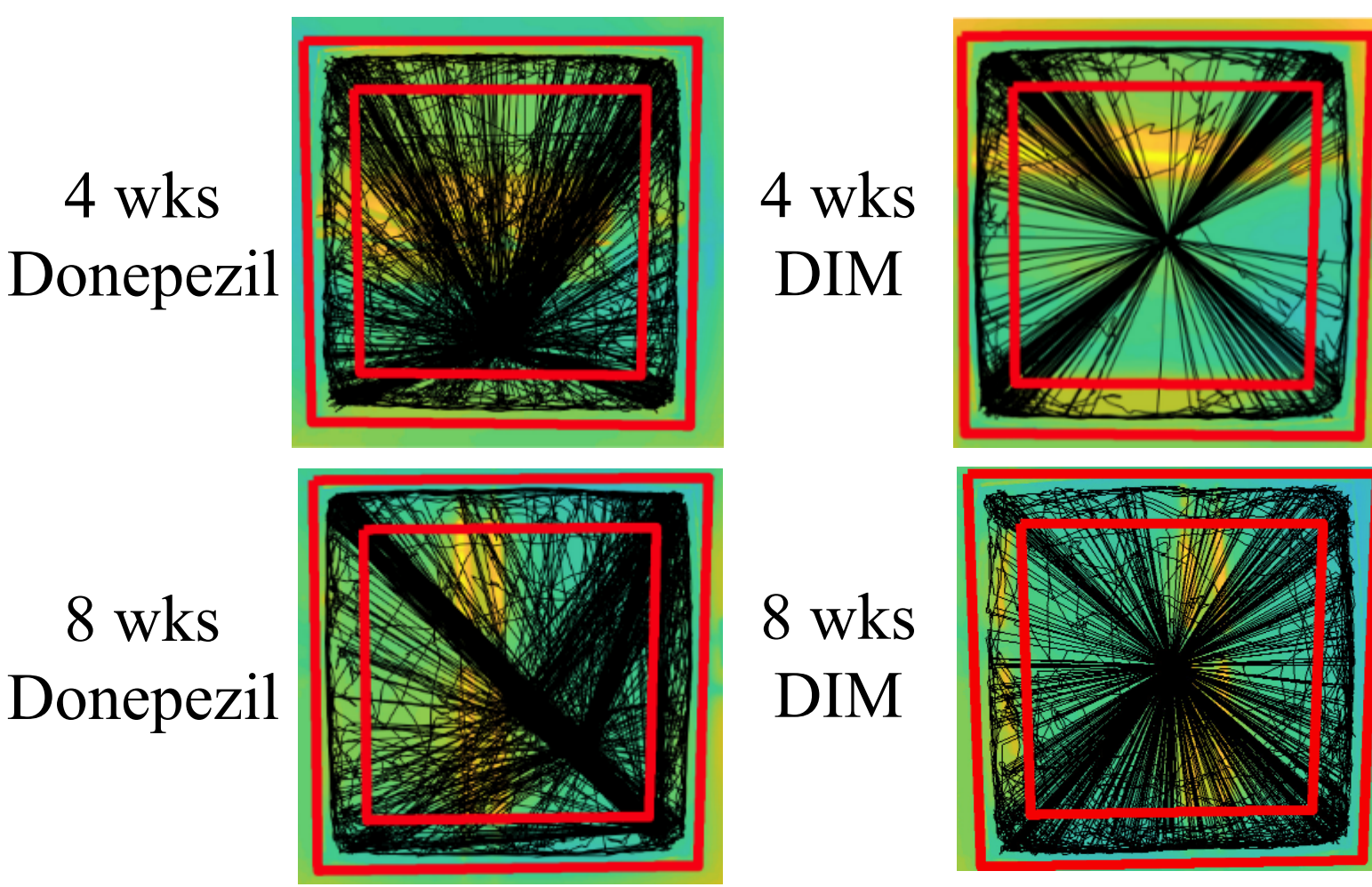
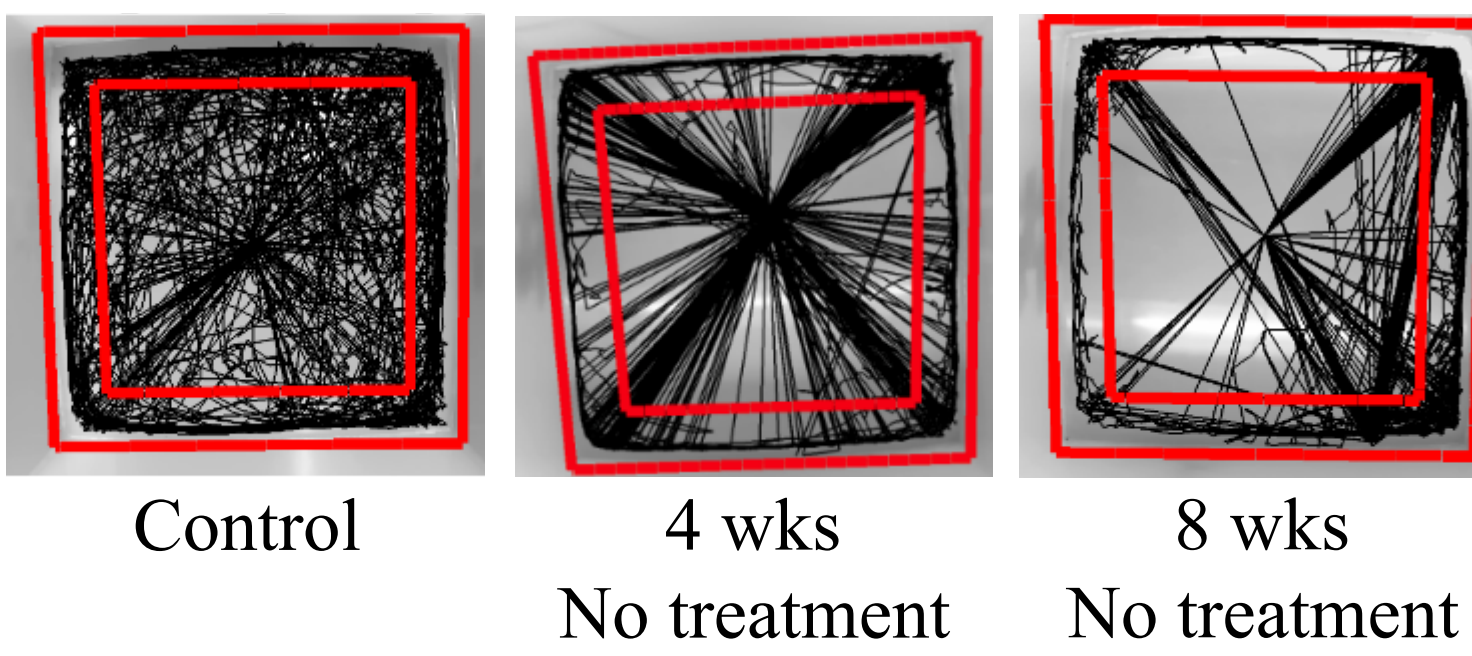


Normal mouse behavior:  
Buries ~11 marbles over 20 min.

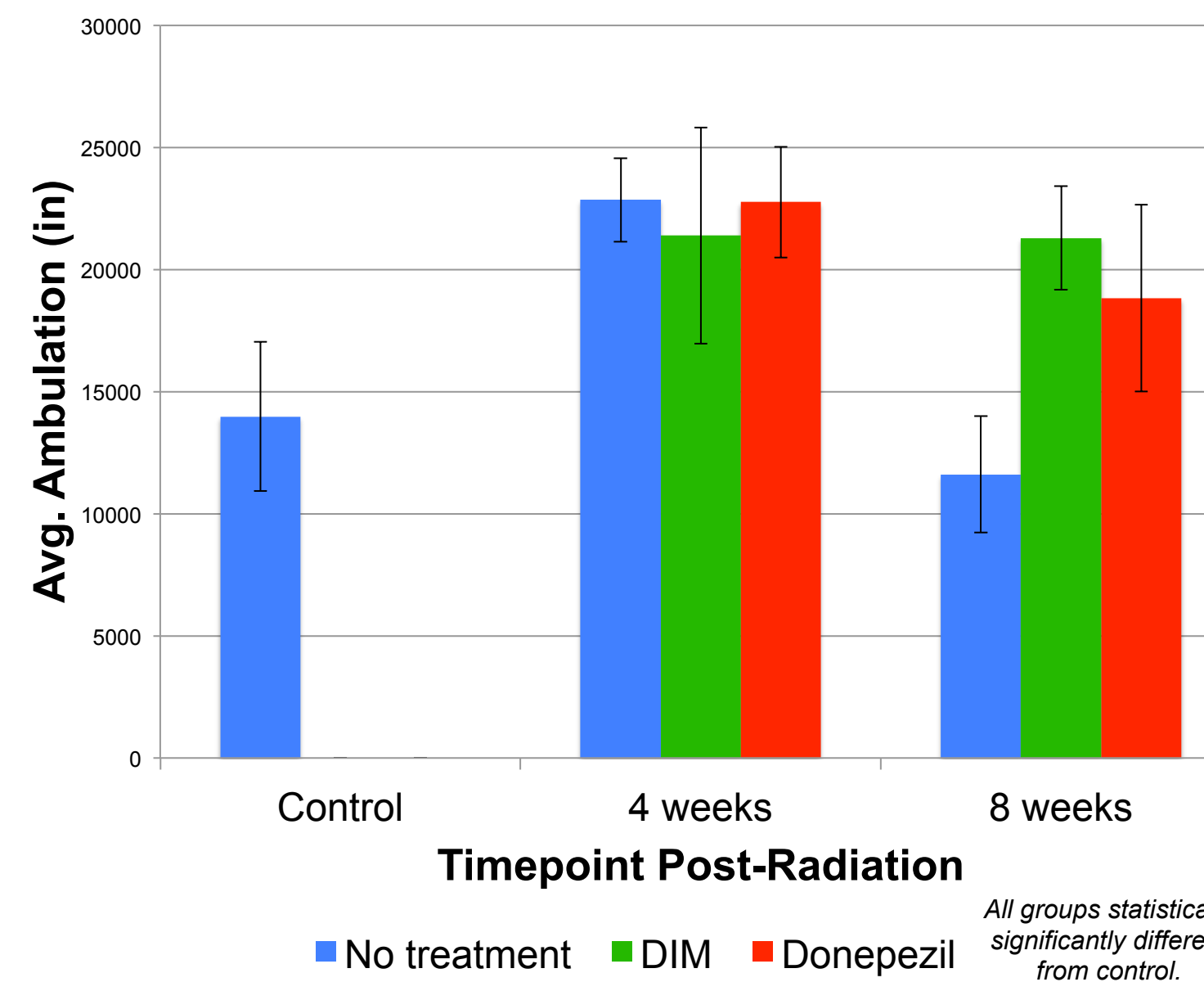
\*Tests chosen for ability to measure anxiety, cognitive abilities, and normal mouse behavior.

## Results

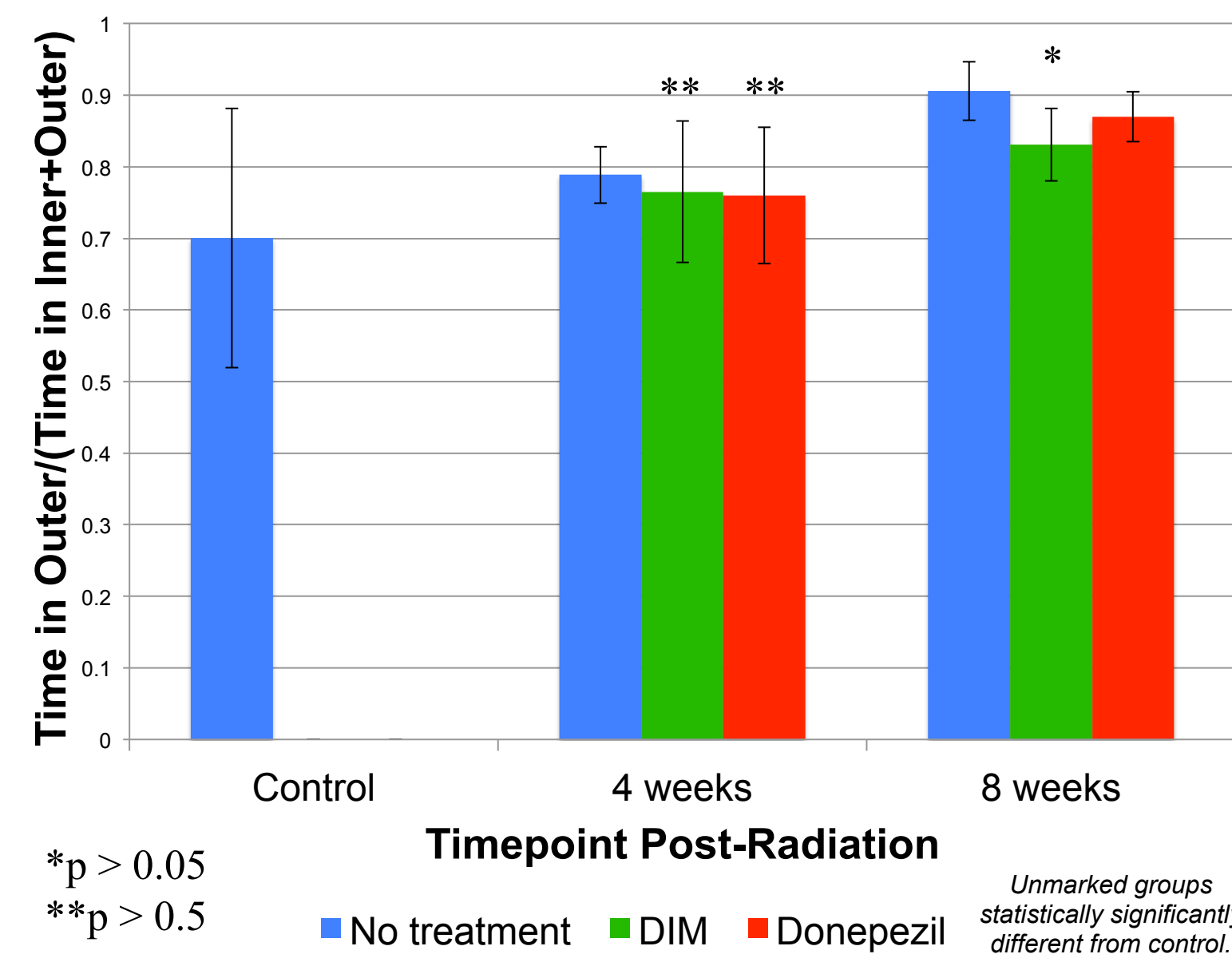
### Open Field Data



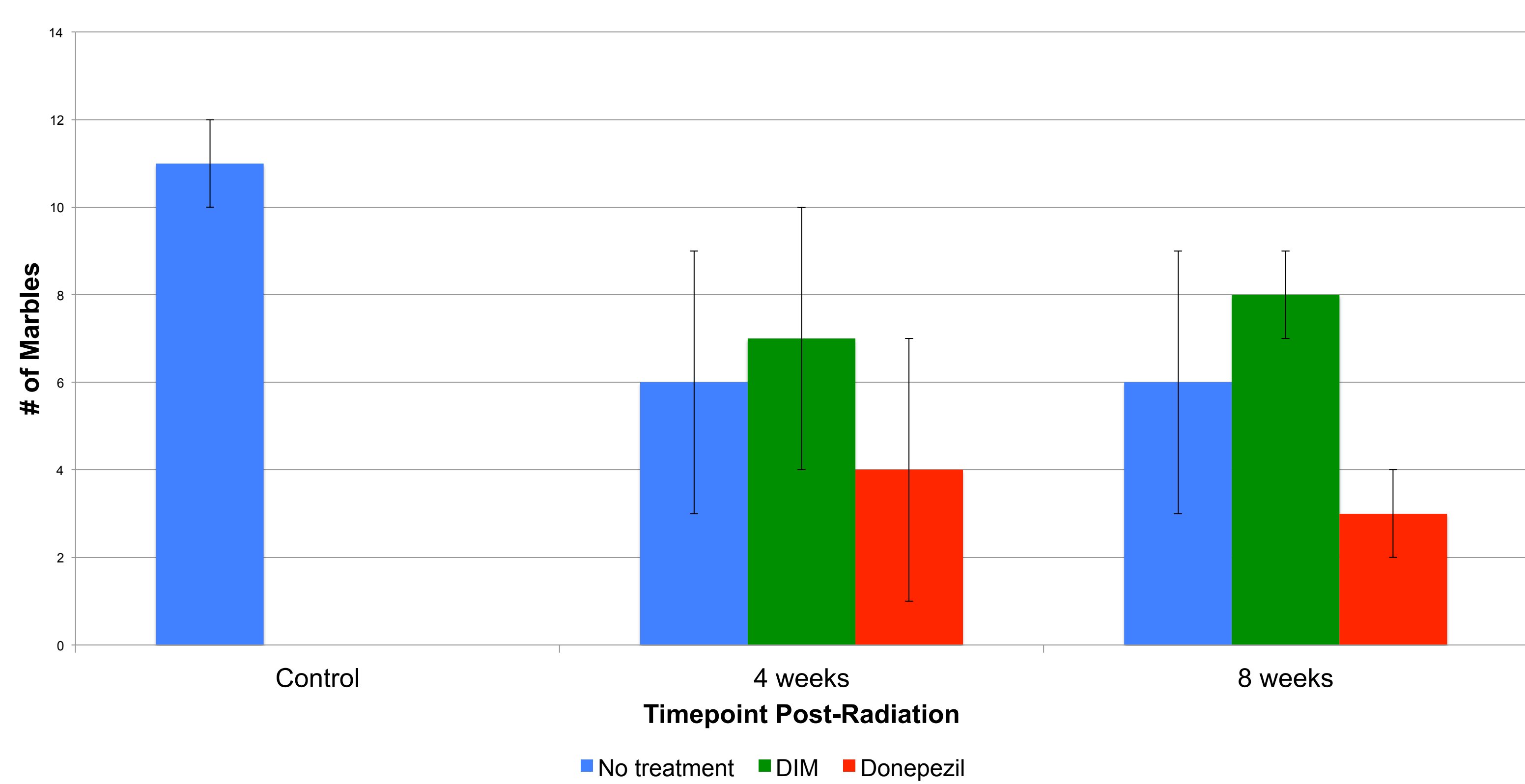
### Average Total Ambulation



### Average Thigmotaxis



### Median Number of Marbles Buried



## Conclusions

- Qualitative observations indicated overall more mobile and healthy mice with the DIM treatment.
- Quantitative results did not support the effectiveness of DIM, but did lessen cognitive impairment for some mice, (outliers skewed results).
- Donepezil was not effective; worsened cognitive impairment.

## Future Directions

- Re-evaluate effectiveness of behavior tests.
- Increase sample size of experiments to get more consistent results.
- Further investigate the use of DIM and understand the drug's mechanisms.
- Develop tumor model for mice.
- Do radioprotectants also protect tumor tissue? Or just healthy tissue?

## Acknowledgements

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